PATENT
Attorney Docket No.: QUIG-1006USCIP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Richard Allen ROSENBLOOM

Serial No.: **10/045,790**

Group Art Unit: **1617**

Filed: **January 14, 2002**

Examiner: **S.A. Jiang, Ph.D.**

For: **ORAL COMPOSITIONS AND METHODS FOR PREVENTION, REDUCTION AND TREATMENT OF RADIATION INJURY**

DECLARATION GERALD H. SOKOL, M.D. PURSUANT TO 37 C.F.R. § 1.132

Assistant Director of Patents & Trademarks
P.O. Box 1450
Alexandria, VA 22312-1450

Sir:

1. I, Gerald H. Sokol, M.D., hereby declare as follows:

2. I am a medical doctor with significant experience in the fields of radiation therapy and drug evaluation research. My *curriculum vitae* are attached hereto as Appendix A.

3. At my direction, a study was undertaken of a test formulation for the radioprotection/treatment of radiation lethality induced by four MEV photons of ionizing radiation in mice.

4. This study utilized two different routes of administration of the study drug, intraperitoneal ("ip"), that is an injection given in the gut of the mouse, and subcutaneously ("sub-q"), an injection given under the skin of the mouse.

5. C3H mice were used for this study. The mice were monitored daily for weight, food consumption, general health and deaths.

6. The test formulation was administered to two treatment groups of eight mice each, and to two treatment groups of five mice each. Two control groups of eight mice each received only vehicle.

7. Administrations given before the day of irradiation of a mouse are referred to as "pre-RT."

8. Administrations given beginning on the day after the day of irradiation of a mouse are referred to as "post-RT."

9. Group 1 ("SQ1") received daily sub-q injections of the treatment formulation for five days pre-RT and one sub-q injection on the day of irradiation.

10. Group 2 ("SQ2") received daily sub-q injections of the treatment formulation beginning on the day of irradiation and continuing for five days post-RT.

11. Group 3 ("IP1") received daily ip injections of the treatment formulation for five days, pre-RT and one ip injection on the day of irradiation.

12. Group 4 ("IP2") received daily ip injections of the treatment formulation beginning on the day of irradiation and continuing for five days, post-RT.

13. Group 5 ("CSQ1") received daily sub-q injections of vehicle only, for five days pre-RT and one sub-q injection on the day of irradiation.

14. Group 6 ("CIP1") received daily ip injections of vehicle only for five days pre-RT, and one ip injection on the day of irradiation.

15. The undiluted test formulation contained the following ingredients.

INGREDIENTS	**SUPPLIER**	**QUANTITY%w/w**
Water		83.79
Alpha Lipoic Acid	Cognis	5.58
**Baking Soda		2.84
Vitamin D_3	BASF	0.36
Sodium Copper Chlorophyllin	PLT	7.43
TOTAL		**100**

** Amount of baking soda needed to dissolve the alpha lipoic acid. Reaction to create salt. Mixture of 66.34% alpha lipoic acid and 33.76% baking soda.

16. To make the undiluted test formulation, the following procedure was utilized by the formulator, A.M. Todd. First the alpha lipoic acid and baking soda were combined. The water was heated to approximately 60^0C and then added at this temperature to the alpha lipoic acid and baking soda mixture. The composition was then mixed to activate the baking soda and to ensure that the alpha lipoic acid was well mixed in the solution. The Vitamin D_3 was then added followed by sufficient mixing to ensure all ingredients were well mixed. The chlorophyllin was then added with additional mixing. Once the chlorophyllin was added and stirred into solution, the entire solution was heated to 70^0C for ten minutes under constant stirring. After the ten-minute stirring period, the foam was allowed to disperse before the solution was poured into bottles.

17. The study was initiated at a dosage of 0.1 cc of test formulation/day. Following severe symptoms of toxicity (lethargy, loss of appetite, death) during the first 48 hours of the study, the formulation and the control were diluted by two parts saline to one part test formulation or control.

18. The final dosage used in the study 0.06 cc of test formulation/day, beginning on day 3, pre-RT.

19. All six groups of animals received 7 gray (LD50 dose) of ionizing radiation on the same day, three hours after administration of the treatment formulation or control on that day.

20. The animals were fed, watered and husbandry performed daily between the hours of 3 p.m. and 7 p.m. Food consumption was observed and significant changes in eating habits were recorded.

21. The mice were weighed as a group, per cage, and the data was recorded along with the pertinent observations. Observations regarding lethargy, severe weight loss, or fatality were reviewed by the project's veterinarian and reported immediately to the project manager. All deaths were recorded. The dead animals were weighed, labeled individually, and frozen for later necropsy.

22. Median survival times were compared using Kaplan-Meier survival analysis. Statistical significance was evaluated by T-tests, log rank, and the Breslow test.

23. The SQ1 cohort that received daily sub-q injections of the test formulation for five days pre-RT, and once on the day of irradiation, showed statistically significant improved survival ($P = 0.01$) than the CSQ1 control group in the Kaplan Meier survival analysis. Importantly, the significance of the results was confirmed by taking into account the equality of survival distributions test by the Log Rank, Breslow, and Tarone-Ware procedures ($P = 0.001$).

24. Clinically significant results were observed in all other treatment groups (see the attached Data Tables in Appendix B).

25. Overall the combined pre-treatment cohort's absolute survival percentage was 55.56% compared to the control of only 6.25%.

26. The highest percentage survival was observed in the post-RT treatment group via ip administration, (80%), which again was a clinically significant outcome relative to the control.

27. In addition to increased absolute survival, both the pre-RT and post-RT groups (except for the post-RT sub-q cohort) exhibited favorable delayed death rates compared to the controls.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that the statements were made with the knowledge that willful false statements and the like made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

By: _____
Gerald H. Sokol, M.D.

Dated: 3/28/05

KAPLAN MEIER SURVIVAL ANALYSIS

Survival Analysis for Pre-XRT SubQ vs Control

Factor compound = 0 (Control)

Time	Status	Cumulative Survival	Standard Error	Cumulative Events	Number Remaining
11	1	.8750	.1169	1	7
13	1			2	6
13	1	.6250	.1712	3	5
14	1			4	4
14	1	.3750	.1712	5	3
16	1			6	2
16	1	.1250	.1169	7	1
21	1	.0000	.0000	8	0

Number of Cases: 8 Censored: 0 (.00%) Events: 8

	Survival Time	Standard Error	95% Confidence Interval
Mean:	15	1	(13, 17)
Median:	14	1	(13, 15)

Survival Analysis for Pre-XRT SubQ Treatment

Factor compound = 1 (Treatment)

Time	Status	Cumulative Survival	Standard Error	Cumulative Events	Number Remaining
17	1			1	5
17	1	.6667	.1925	2	4
20	1	.5000	.2041	3	3
21	0			3	2
21	0			3	1
21	0			3	0

Number of Cases: 6 Censored: 3 (50.00%) Events: 3

	Survival Time	Standard Error	95% Confidence Interval
Mean:	20	1	(18, 21)
(Limited to	21)		
Median:	20		(.,)

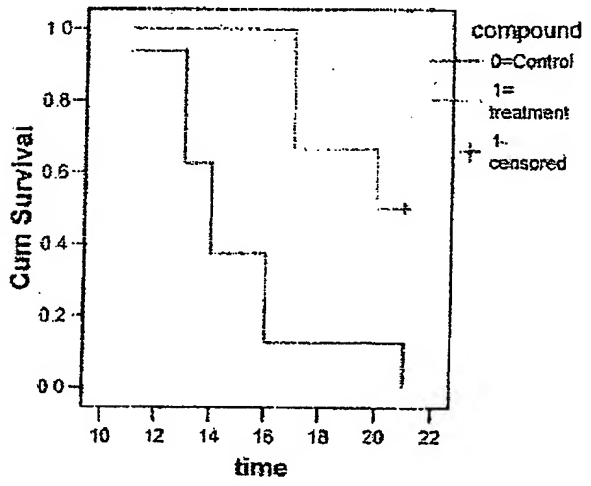
Survival Analysis for time

		Total	Number Events	Number Censored	Percent Censored
compound (Control)	0	8	8	0	.00
compound (Treatment)	1	6	3	3	50.00
Overall		14	11	3	21.43

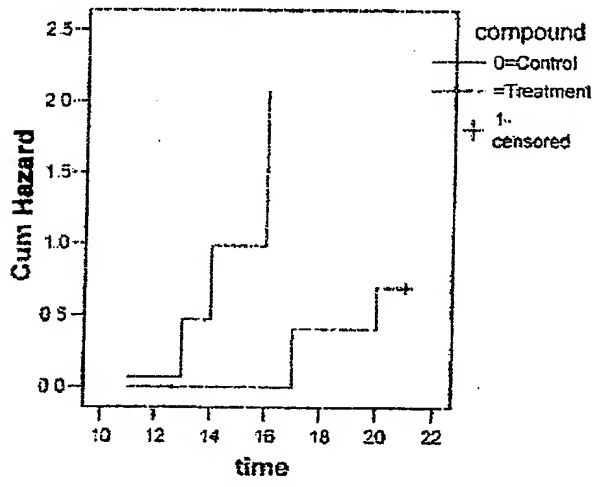
Test Statistics for Equality of Survival Distributions, pre-XRT SubQ treatment.

	Statistic	df	Significance
Log Rank	7.82	1	.0052
Breslow	7.75	1	.0054
Tarone-Ware	7.96	1	.0048

Survival Function for Pre-XRT SubQ Rx vs Control



Hazard Function for Pre-XRT SubQ Rx vs Control



Survival Analysis for Pre-XRT IP Rx vs Control

Factor Compound = 0 (Control)

Time	Status	Cumulative Survival	Standard Error	Cumulative Events	Number Remaining
12	1	.8750	.1169	1	7
13	1	.7500	.1531	2	6
14	1	.6250	.1712	3	5
16	1			4	4
16	1	.3750	.1712	5	3
17	1	.2500	.1531	6	2
20	1	.1250	.1169	7	1
23	0			7	0

Number of Cases: 8 Censored: 1 (12.50%) Events: 7

	Survival Time	Standard Error	95% Confidence Interval	
Mean:	16	1	(14,	19)
(Limited to	23)			
Median:	16	1	(13,	19)

Survival Analysis for time

Factor Compound = 1 (treatment)

Time	Status	Cumulative Survival	Standard Error	Cumulative Events	Number Remaining
14	1	.6667	.2722	1	2
23	0			1	1
23	0			1	0

Number of Cases: 3 Censored: 2 (66.67%) Events: 1

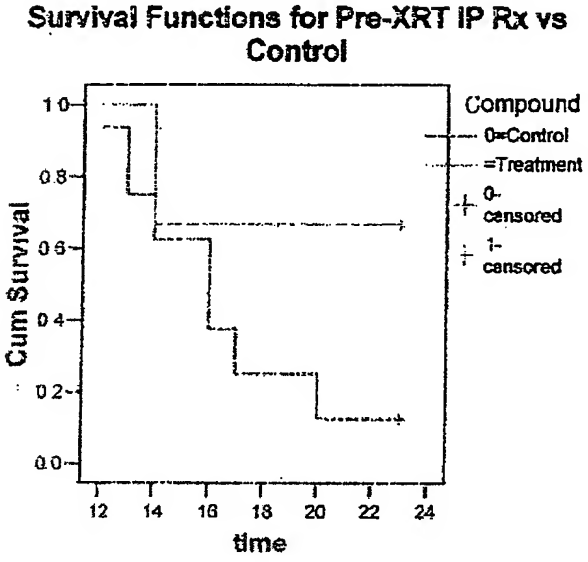
	Survival Time	Standard Error	95% Confidence Interval	
Mean:	20	2	(15,	25)
(Limited to	23)			
Median:	.	(	.,	)

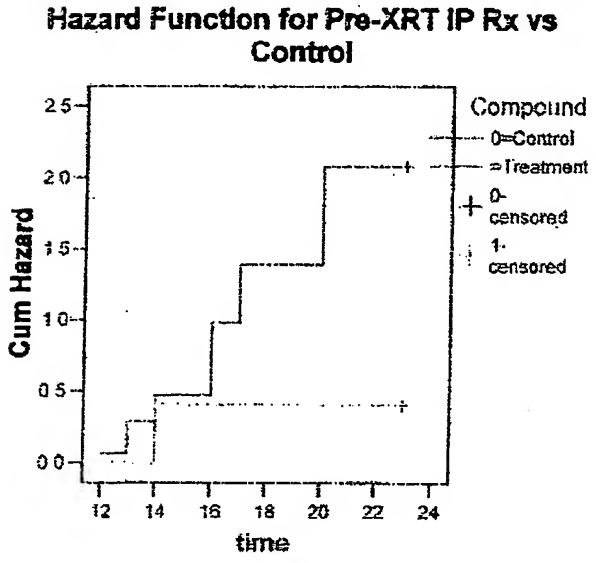
Survival Analysis for Pre-XRT IP Rx vs Control

		Total	Number Events	Number Censored	Percent Censored
Compound	0	8	7	1	12.50
Compound	1	3	1	2	66.67
Overall		11	8	3	27.27

Test Statistics for Equality of Survival Distributions for Pre-XRT IP Rx vs Control

	Statistic	df	Significance
Log Rank	1.80	1	.1799
Breslow	1.17	1	.2788
Tarone-Ware	1.47	1	.2257





Survival Analysis for Post XRT SubQ Rx vs Control

Factor compound = 0 (Control)

Time	Status	Cumulative Survival	Standard Error	Cumulative Events	Number Remaining
11	1	.8750	.1169	1	7
13	1			2	6
13	1	.6250	.1712	3	5
14	1			4	4
14	1	.3750	.1712	5	3
17	1			6	2
17	1	.1250	.1169	7	1
21	1	.0000	.0000	8	0

Number of Cases: 8 Censored: 0 (.00%) Events: 8

	Survival Time	Standard Error	95% Confidence Interval
Mean:	15	1	(13, 17)
Median:	14	1	(13, 15)

Survival Analysis for time

Factor compound = 1 (Treatment)

Time	Status	Cumulative Survival	Standard Error	Cumulative Events	Number Remaining
10	1	.8000	.1789	1	4
11	1	.6000	.2191	2	3
13	1			3	2
13	1	.2000	.1789	4	1
21	0			4	0

Number of Cases: 5 Censored: 1 (20.00%) Events: 4

	Survival Time	Standard Error	95% Confidence Interval
Mean:	14	2	(10, 17)
(Limited to	21)		
Median:	13	1	(11, 15)

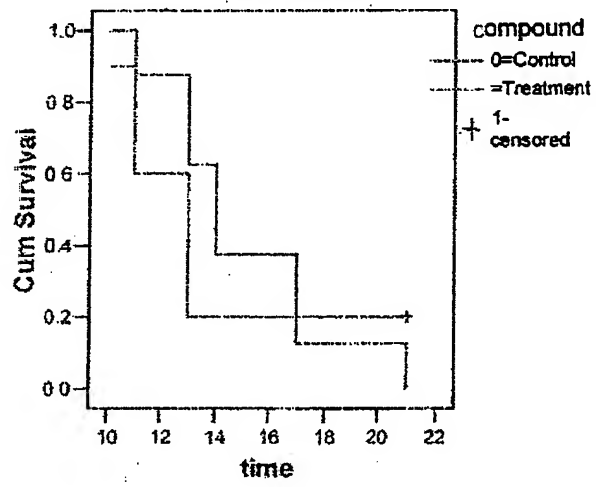
Survival Analysis for time

		Total	Number Events	Number Censored	Percent Censored
compound	0	8	8	0	.00
compound	1	5	4	1	20.00
Overall		13	12	1	7.69

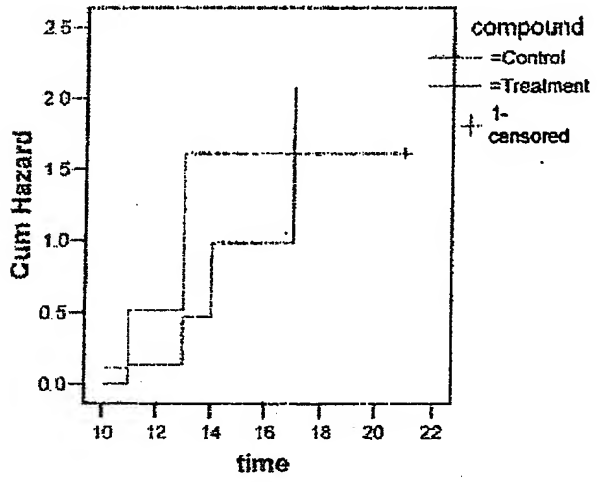
Test Statistics for Equality of Survival Distributions for Post-XRT SubQ Rx vs Control

	Statistic	df	Significance
Log Rank	.09	1	.7645
Breslow	1.35	1	.2460
Tarone-Ware	.70	1	.4034

Survival Functions for Post-XRT SubQ Rx vs Control



Hazard Function for Post-XRT SubQ Rx vs Control



Survival Analysis for Post XRT IP Rx vs Control

Factor Compound = 0 (Control)

Time	Status	Cumulative Survival	Standard Error	Cumulative Events	Number Remaining
12	1	.8750	.1169	1	7
13	1	.7500	.1531	2	6
14	1	.6250	.1712	3	5
16	1			4	4
16	1	.3750	.1712	5	3
17	1	.2500	.1531	6	2
20	1	.1250	.1169	7	1
23	0			7	0

Number of Cases: 8 Censored: 1 (12.50%) Events: 7

	Survival Time	Standard Error	95% Confidence Interval	
Mean:	16	1	(14,	19)
(Limited to	23)			
Median:	16	1	(13,	19)

Survival Analysis for time

Factor Compound = 1 (Treatment)

Time	Status	Cumulative Survival	Standard Error	Cumulative Events	Number Remaining
12	1	.8000	.1789	1	4
23	0			1	3
23	0			1	2
23	0			1	1
23	0			1	0

Number of Cases: 5 Censored: 4 (80.00%) Events: 1

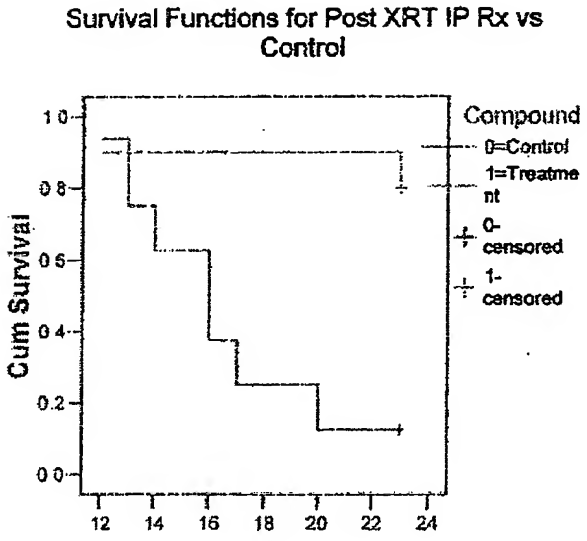
	Survival Time	Standard Error	95% Confidence Interval	
Mean:	21	2	(17,	25)
(Limited to	23)			
Median:	.		(	)

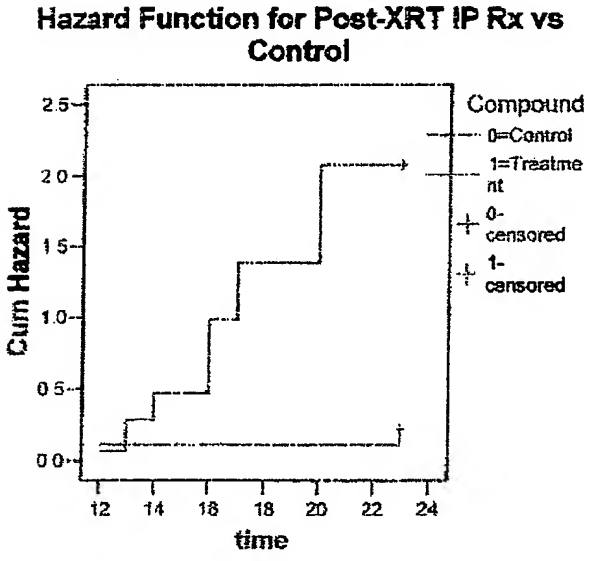
Survival Analysis for time

		Total	Number Events	Number Censored	Percent Censored
Compound	0	8	7	1	12.50
Compound	1	5	1	4	80.00
Overall		13	8	5	38.46

Test Statistics for Equality of Survival Distributions for Post XRT IP Rx vs Control

	Statistic	df	Significance
Log Rank	3.92	1	.0477
Breslow	2.45	1	.1179
Tarone-Ware	3.17	1	.0751





DATA TABLES

IP-CONTROL-Pre XRT

Day	# Alive	Avg. Wt.	Comments
1	8	216	inj .06
2	8		inj .06
3	8	219	inj .06
4	8		inj .06
5	8	219	inj .06
6	8		Day of XRT, inj .06
7	8	220	
8	8		
9	8	221	
10	8		
11	8	221	
12	7		1 death
13	6		1 death
14	5	129	1 death
15	5		
16	3	91	2 deaths
17	2		1 death
18	2	59	
19	2		
20	1		1 death
21	1		

IP-TREATMENT -Pre XRT

Day	# Alive	Avg. Wt	Comments
1	3	81	2:1 dil after 5 deaths. Chg
2	3		to .06
3	3	84	
4	3		inj .06
5	3	86	inj .06
6	3		Day of XRT, inj .06
7	3	86	
8	3		
9	3	85	
10	3		
11	3	86	
12	3		
13	3		
14	2	53	1 death
15	2		
16	2	53	
17	2		
18	2	52	
19	2		
20	2	26	
21	2	55	

NOTE: Day 1 is first day of "arrived at" dosage.

SubQ-CONTROL - Pre XRT

Day	# Alive	Avg. Wt.	Comments
1	8	237	inj .06
2	8		inj .06
3	8	248	inj .06
4	8		inj .06
5	8	246	inj .06
6	8		Day of XRT, inj .06
7	8	240	
8	8		
9	8	233	
10	8		
11	7	200	1 death
12	7		
13	5	40	2 deaths
14	3	86	2 deaths
15	3		
16	3	84	
17	1		2 deaths
18	1		
19	1		
20	1		
21	0		1 death

SubQ-TREATMENT - Pre XRT

Day	# Alive	Avg. Wt	Comments
1	6	184	inj .06
2	6		inj .06
3	6	185	inj .06
4	6		inj .06
5	6	181	inj .06
6	6		Day of XRT, inj .06
7	6	178	
8	6		
9	6	176	
10	6		
11	6	174	
12	6		
13	6		
14	6	171	
15	6		
16	6	169	
17	4		2 deaths
18	4	107	
19	4		
20	3		1 death
21	3	76	

NOTE: Day 1 is first day of "arrived at" dosage.

SubQ -TREATMENT - Post XRT

Day	# Alive	Avg Wt	Comments
1	5		XRT-7Gy and
2	5	133	inj .06 day of and x 5 days
3	5		
4	5	130	
5	5		
6	5	129	
7	5		
8	5	128	
9	5		
10	4		1 death
11	3	72	1 death
12	3		
13	1	28	2 deaths
14	1		
15	1	26	
16	1		
17	1		
18	1	23	
19	1		
20	1	21	
21	1		
22	1	22	
23	1		

IP-TREATMENT - Post XRT

Day	# Alive	Avg Wt	Comments
1	5		XRT-7Gy and
2	5	126	inj .06 day of and x 5 days
3	5		
4	5	127	
5	5		
6	5	126	
7	5		
8	5	125	
9	5		
10	5		
11	5	124	
12	4		1 death
13	4	102	
14	4		
15	4	97	
16	4		
17	4		
18	4	99	
19	4		
20	4	100	
21	4		
22	4	102	
23	4		

COMBINED GROUP DATA

CONTROL			TREATMENT	
Day		Comments	Day	Comments
1			1	
2			2	
3			3	Adj. due to lethality
4			4	
5			5	
6			6	
7			7	
8			8	
9			9	
10			10	
11			11	
12			12	
13			13	
14			14	
15			15	
16			16	
17			17	
18			18	
19			19	
20	2		20	
21	1		21	

APPENDIX A

CURRICULUM VITAE

NAME Gerald H. Sokol, M.D.

EDUCATION

1965	AB Indiana University and Temple University, Indianapolis IN, Philadelphia, PA
1968	MS (Pharmacology) Indiana University, Indianapolis, IN
1970	MD Indiana University, Indianapolis, IN; combined Degree Program in Experimental Science (upper 10%)
1970-1971	Internship, Temple University, Philadelphia, PA
1971-1973	Residency in Internal Medicine, USPHS Hospital in affiliation with Johns Hopkins University, the University of Maryland, Baltimore, MD and NCI
1973-1976	Resident, Massachusetts General Hospital; and Fellow, Harvard Medical School, Radiation Medicine/Oncology
1976-1977	Fellow, Clinical Pharmacology, Massachusetts General Hospital, Harvard Medical School

CURRENT PROFESSIONAL POSITIONS

1990-	Director of Oncology, New Hope Cancer Center
1990-2001	Vice Chief of Radiation Therapy, Tampa General Hospital
1987-	Officer, Center for Drug Evaluation Research, FDA
1990- 2001	President, Okaloosa Radiation Therapy Oncology Center
2000-2001	Staff Physician-H. Lee Moffitt Cancer Center, Tampa, Fl.
2002-	Special Volunteer, National Cancer Institute.

BOARD CERTIFICATION

1972	American Board of Internal Medicine #44334
1976	American Board of Radiology (Therapeutic Radiology)
1977	American Board of Internal Medicine Sub-specialty Oncology
1991	American Board of Clinical Pharmacology
1992	American Board of Quality Assurance #30431

MEDICAL LICENSURE

1975	Florida ME0025907
1987	Washington DC

HONORS/AWARDS

1970	Upper 13% of Medical Class
1968	Pittman-Moore Fellow
1965	Little '500' Scholar Health Professions Scholars
1965	AEO Honorary Premedical Fraternity
1965	Long Island Home Scholarship
1973	Fellow, American Cancer Society
1982-1986	National Scientific Advisory Board, Janssen Pharmaceutica
1985	American Cancer Society Board of Directors
1087	10 Year US Government Service Award
1992	Fellow, American College of Clinical Pharmacology
1997	FDA Performance Award
1998	FDA Award for Drug Review

PREVIOUS PROFESSIONAL POSITIONS

1973-1977	Assistant Physician in Medicine, Peter Bent Brigham Hospital, Boston, MA
1976-1977	Assistant Professor, Tufts University School of Medicine, Therapeutic Radiology, Boston, MA
1977-1978	Director, Radiation Oncology, Radiation Therapy Oncology Center at Mease Hospital, Dunedin, FL
1978-1989	Director, Radiation Oncology, Tampa General Hospital, Tampa, FL
1979-	President, Tampa Scientific Association, Tampa, FL.
1985	Associate Director, Clinical Research, Schering-Plough Pharmaceutical, Kenilworth, NJ
1987-	Research Review Officer, Center for Drug Evaluation and Research, FDA, USUHS,Rockville, MD

1987-1990	Director, Radiotherapy, Columbia Hospital for Women
1990-2001	Vice Chief, Radiation Oncology, Tampa General Hospital
1992-1995	Vice President Medical Affairs/Director Medical Education, Prince George's Hospital Center, Cheverly, MD
1997-1998	Medical Director, Chief Medical Officer - MetSolutions (a Bozel world-wide Company - Company acquired)

PROFESSIONAL SOCIETIES

1968	Society of Sigma XI, Honorary Scientific Society, American Medical Association
1972	New York Academy of Science
1977	American Society of Clinical Oncology
1980	Florida Society of Clinical Oncology
1977	American Society of Therapeutic Radiology
1977-1979	American Society of Internal Medicine
1980-	American Society of Clinical Pharmacology
1980	National Association of Advancement in Science
1977	American College of Radiology
1982-1987	Liaison Fellow American College of Surgery
1985-1995	State Representative Presidential Advisory Committee
1980-1992	Southern Medical Association
1980-	American College of Clinical Pharmacology
1982-	Radiation Research Society
1983-	North American Hyperthermia Group
1984-	American Medical Association
1985-	Washington DC Medical Society

USUHS TEACHING ACTIVITIES

Commanding Officer - US Naval Reserve Unit at USUHS (1997-1999)
Clinical Pharmacology Staff- Consulting Service, Naval Hospital, Bethesda (1990-present)
Research Activities - Current Studies

Trimetrexate for Colon Cancer
Renal Functions associated with Reno-toxic drugs (1998)
Troponin levels s/p cardiac chemo/XRT (1999)
Community Clinical Pharmacology Outreach Program (initiated 1999)
Co-investigator cocaine antagonist PK study.
PI oxandrolone cancer cachexia study.
PI Community Outreach Clinical Pharmacology project.

PI Pharmacy DUR Study-Now and Stat Order Study
Carbonic Anhydrous Enzyme Activity Study (paper in press British Journal of Pharmacology)
Medico legal - Medical Jurisprudence Project (1999)
Two weeks Navy Reserve (1995-2002)- Division of Clinical Pharmacology
Clinical Pharmacology course lecturer 1990- present
Pharmacology Course lecturer 1990 – present
International Teaching Conferences. Army Update, Wiligen, Germany; Taiwan Government Drug Review Seminar, 1995
Yearly Clinical Pharmacology course, teaching and lecturing lab and course lecture, preparation of course curriculum handout.
Coverage of Clinical Pharmacology Research Unit, including weekend call.
Journal Club Coordinator-Clinical Pharmacology Fellowship Training Program

EDITORIAL ACTIVITES

1996-	Clinical Trials Advisor-Editorial Board
1996-1997	Oncology Management
2000-	Reviewer, Internet Journal of Medical Toxicology
2002-	Chronic Lung Disease/Emphysema-Editorial Advisor

OTHER PROFESSIONAL ACTIVITIES

FDA Consultant to Office of Compliance, General Council, and Devices 1992 -
P.T. Committee - Bayonet Regional Medical Center 1998-
Cancer Committee - Bayonet Regional Medical Center 1998-
Chief Medical Officer, MedMatRx 1998-99
Member, Pediatric Oncology Group 1981-1987
Member South West Oncology Group 1981-1987
Program Director and Coordinator - University Cancer Study Group Update 1981
Chairman, Institutional Review Board, Tampa General Hospital, University of South Florida 1981-1984
Chairman, Hyperthermia/Chemotherapy Oncology Study Group 1986-1988
Member, Institutional Review Board, Tampa General Hospital 1991-1993
National Oversight, Public Health Service, Quality Control Committee 1991-1995
VA Peer Review Committee - VA Hospital System 1993-1996
FDA Oncology Advisory Panels, NCI Consensus Conference NCI Phase I Meeting, 1989, 1990, 1994, 1996,
FDA Representative to Radiation Sensitizer NCI Meeting 2002

FDA Representative-Oncology Drug Develop Symposium-panelist, Georgetown University/NCI February, 2003

GRANTS

1. Tigan Radiation and Chemotherapy Antiemetic Study - Beecham Laboratories - $25,000, 1982-1986, G.H. Sokol, MD, Principal Investigator.

2. Ciramodaol - Agonist-Antagonist Analgesic for Cancer Pain - Wyeth Laboratories - $15,000. 1983 G.H. Sokol, MD, Principal Investigator.

3. Leuprolide LH-FSH-RH Agonist for Breast Cancer - Abbott Laboratories - $10,000, 1984-1985, G.H. Sokol, MD, Principal Investigator.

4. Leuprolide LH-FSH-RH Agonist for Prostate Cancer - Abbott Laboratories - $46,000, 1984-1986, G.H. Sokol, MD. Principal Investigator

5. Phase I Study of Unique C-Parvum Derivative - ImmunoMed Inc. - $45,000, 1983, G.H. Sokol, MD Principal Investigator

6. Comparative Efficacy of Metoclopramide vs. Compazine vs. Placebo in Radiation Induce Nausea A.H. Robins, Inc - $45,000, 1983-1985, G.H. Sokol, MD Principal Investigator

7. Buprenorphine - Sublingual Administration in Chronic Cancer Pain - Med Tech Research, Inc.- $20,000, 1985, G.H. Sokol, MD Principal Investigator

8. Imodium - Placebo Controlled Study in Radiation Induced Diarrhea - Janssen Pharmaceutica - $14,000, 1985, G.H. Sokol, MD Principal Investigator

9. H.D. Nizoral in New and Hormonally Failed Prostatic Carcinoma - Janssen Pharmaceutica - $150,000, 1985, G.H. Sokol, MD Principal Investigator

10. Letrazol for Advanced Adjuvant Breast Cancer - Novartis - $20,000, 1986, G.H. Sokol, Principal Investigator

11. Trimetrexate with/without 5-FU/leucovorin for 2nd line colon cancer treatment, US BioScience,- $15,000, 1999, G.H. Sokol, MD Principal Investigator

12. Erythropoietin for anemia associated with radiation therapy, Ortho Biotech - $15,000, 1999, G.H. Sokol, MD Coinvestigator

13. Oxandrolone Weight Gain Study for Oncology Patients-$18,000, 2001-2002, G. H. Sokol PI

14. Free Radical Scavengers as Radioprotectors in Mice-$102,000, 2002 G.H. Sokol PI

INVITED AND EXTRAMURAL PRESENTATIONS

1. American Cancer Society Cancer Review - Chemotherapy of G.U. and GYN malignancy, Tampa, Fl. 1977
2. Lecturer, Clinical Pharmacology University of South Florida School of Medicine, Tampa, Fl., 1978
3. Clinical Pharmacology Course, Tampa, Fl. 1978
4. Prostate Cancer, Mease Hospital, Dunedin, Fl., 1978
5. New Developments in Cancer, Morton Plant Hospital, Clearwater, Fl., 1978
6. University of South Florida Grand Rounds - New Approaches to Breast Cancer, Tampa, Fl., 1979
7. American Cancer Society Seminar - Channel 8 - Tampa, Health Effects of Smoking, Tampa, Fl. 1979
8. National Conference of Radiation Technology - Radiobiology- Coordinator, Tampa, Fl. 1979
9. Kiwanis Club Dunedin - New Developments in Cancer, Dunedin, Fl. 1979
10. University Cancer Study Group – Coordinator and Moderator, Clearwater, Fl. 1981
11. Immunotherapy in Cancer Treatment. Oncology Grand Rounds, Tampa, Fl. 1981
12. Update of Breast Cancer, Memorial Hospital, Tampa, Fl., 1981
13. Extracorporeal Irradiation of Blood in Kidney. Channel 44-Tampa, Fl. 1982
14. 2nd and 3rd Annual University Cancer Study Group Updates – Coordinator and Moderator, Clearwater, Fl. 1983, 1985
15. Hyperthermia in Cancer Treatment - Florida State Oncology Nursing Association and American Cancer Society, Tampa, Fl. 1984

16. Control of Cancer Pain - Coordinator and Moderator- American Cancer Society and University of South Florida, Tampa, Fl. 1984

17. Pharmacology and Analgesics. American Cancer Society, Tampa, Fl. 1984

18. Leuprolide-A new Drug for Prostate Cancer. Channel 13 Tampa, Fl. 1984

19. Radiation Oncology Update. Florida Keys Hospital, Key West, Fl. 1985

20. The Interaction of Hyperthermia and Chemotherapy in Cancer Management. BSD. Florida Symposium on Hyperthermia, Tampa, Fl. 1985

21. Hyperthermia in Cancer Management. Florida Society of Radiologic Technologists. Tampa, Fl. 1985

22. Buprenorphine-A New Pain Killer for Cancer Patients Channell 44 Tampa, Fl. 1985

23. New Developments in Head and Neck Cancer. University of South Florida 1985.

24. Oncologic Drugs Lecture Series. Georgetown University, Washington, DC 1987

25. Radiation Drug Interactions. George Washington University, Washington, DC 1987

26. Annual Nursing Conference, Oncologic Staging. Tampa, FL 1987

27. New Development in Cancer Treatment. TV-BLAB, Pensacola, Fl. 1987

28. Medical Ethics. University of West Florida, Pensacola, Fl. 1987

29. Psychopharmacology and Religion. University of West Florida, Pensacola, Fl. 1987

30. Medical Effects of Ionizing Radiation (monthly). USUHS, Bethesda, MD 1985

31. Washington, DC, Capitol Hill Hospital. Update of Radiation Oncology. Washington, DC Columbia Hospital for Women, New Development in GYN Oncology. Rockville, MD, FDA Medical Advisory Committee. Oncology Ifosphamide and Mesna NDA Reviews. Rockville MD. 1988

32. Food Irradiation, Stereotactic Radiation Therapy. Florida Society of Radiation Technologist, Tampa, Fl. 1989

33. Radiation Effects of Drug Disposition. FDA-Staff College, Rockville, MD 1990

34. Conference on Quality of Life in Cancer Treatment. NCI-FDA, Bethesda, MD 1990

35. Oncology Review Course. American College of Clinical Pharmacology, Rockville, MD 1991

36. Radiation Oncology Update. Bayonet Point Regional Medical Center, Hudson, Fl. 1991

37. Effects of Radiation on Drug Disposition, USUHS. Bethesda, MD 1991

38. Food Irradiation, Promises for the Future. Public Television, Tampa, Fl. 1991

39. Head and Neck Cancers, Thyroid Cancer, Sarcomas. Tumor Board, Bayonet Point Regional Medical Center, Hudson, Fl. 1991

40. Radiation Drug Interaction Regulatory Aspects Center, Rockville, MD 1991

41. Hyperthermia in Cancer Treatment-Coordinator and Moderator. American Cancer Society Seminar,1991

42. New Developments in Radiation Oncology. American Cancer Society Seminar and University of South Florida - Interuniversity Conference, Tampa, Fl. 1991

43. Tumor Board. Bayonet Point Regional Medical Center, Hudson, Fl. 1992

44. Principles of Oncology. US Navy-Bethesda Naval Hospital, Bethesda, MD 1992

45. Sokol, G.H., Murgo, A., and Cantilena, L. Geriatric Issues Pertaining to Quality of Life in the Regulatory Evaluation of Drugs-An Oncology Perspective. National Symposium on Drugs, Drug Companies, and Quality of Life Issues: Quality of Life Studies and Regulations. New York, NY, October 22, 1992

46. Principles of Radiation Oncology. Prince George's Hospital Center, Cheverly, MD 1993

47. Cost Effective Rationale Therapeutics, Prince George's Hospital Center, Cheverly, MD 1993

48. Ethical and Rational Therapeutics. Touro Clinic, New Orleans, LA 1993

49. Regulatory Aspects vs. Cost Effectiveness vs. Ethics in Drug Care, FDA, Rockville, MD 1994

50. Cancer of the Ovary. Prince George's Hospital, Cheverly, MD 1994

51. Decision Making in the Drug Selection Process. Armed Forces Institute of Pathology, Silver Spring, MD 1994

52. Clinical Pharmacology Seminar - Radiation Drug Interaction - Radiation Effects on The Disposition of Drugs. Uniformed Services University of the Health Sciences, Bethesda, MD 1994

53. Sarcomas. Tumor Board. Bayonet Point Regional Medical Center, Hudson, Fl. 1994

54. Merckle Cell Tumors. Tumor Board. Bayonet Point Regional Medical Center, Hudson, Fl. 1994

55. Principles of Ethical Drug Therapeutics. US Navy USUHS Unit, Bethesda, MD

56. Principles of Gynecologic Oncology. (cervical cancer, endometrial cancer) Prince George's Hospital Center, Cheverly, MD 1994

57. Oncologic Emergencies. Prince George's Hospital Center, Cheverly, MD 1994

58. Principles of Gynecologic Oncology. (ovarian, vulvar cancer) Prince George's Hospital Center, Cheverly, MD 1995

59. Risks and Benefits of Food Irradiation. Division of Clinical Pharmacology USUHS, Bethesda, MD 1995

60. Stroke and CNS Metastatic Disease-Differential Diagnosis, Impact, and Support Measures. Institute of Life Threatening Disease Columbia University NYC, NY. 1995

61. Medical Legal Issues in Clinical Pharmacology-Case Examples. Division of Clinical Pharmacology USUHS, Bethesda, MD. 1995

62. Multiple Lectures to Church and Civic Groups on New Developments in Oncology and Oncologic Drugs. 1995

63. Multiple Presentations to Oncology Drug Products Division FDA on New Drugs and Drug Protocols. Rockville, MD 1995

64. Lymphomas-Diagnosis and Treatment. Tumor Board. Bayonet Point Regional Medical Center, Hudson, Fl. 1995

65. Regulatory Aspects of Drug Development. Protocol Review Techniques. Cost Benefit/Effectiveness Issues in Drug Development. Natl. Taiwan Government Intern Conference on Drug Development. University of Taiwan, Taipei 1995

66. Chronobiologic Implications for PK, New Developments in Clinical Pharmacology, Pharmacoeconomic Principles. Annual 7th Army Continuing Education Symposium Wiligen, Germany 1995

67. Conference on Drugs and Regulatory Overview-Chronobiology-Research, Therapeutic and Regulatory Concerns. Institute for Life Threatening Illness, Columbia University, NYC, NY 1996

68. Chronobiologic Implications for Drug Research, FDA Oversight and Therapeutic Optimization. Grand Rounds, Rockville, MD. 1996

69. Hyperbaric Oxygen-The good, the bad and the ugly. Grand Rounds. Bayonet Point Regional Medical Center, Hudson, Fl. 1996

70. Conference on Apoptosis-Radiation and Modulated Radiation Effects on Apoptosis. Institute for Life Threatening Illness, Columbia University, NYC, NY 1997

71. New Developments in Oncology. Television Station BLAB Sarasota, FL. 1997

72. National Conference on Blood Vessel Irradiation, Washington, DC. FDA Panelist Regulatory Concerns of Blood Vessel Irradiation. 1997

73. Thyroid Cancer, Diagnosis and Treatment. Tumor Board. Bayonet Point Regional Medical Center, Hudson, FL. 1997

74. Reasons for Medical Malpractice. Committee of 100, Williamsburg, VA. 1997

75. New Lymphoma Classifications. Tumor Board. Bayonet Point Regional Medical Center, Hudson, Fl. 1998

76. Conference on Terminal Care in Non-cancer Diseases. Institute of Life Threatening Diseases, Columbia University, NYC. NY 1998

77. New Development of Cancer Treatment. American Cancer Society, New Port Richey, Fl. 1998

78. The Management of Affective Disorders in Cancer Patients. Institute for Life Threatening Illness Columbia University, NYC, NY. 1998

79. Multiple Presentation-Tumor Board. Head and Neck Cancer, Sarcomas, Rectal Cancer. Bayonet Point Regional Medical Center, Hudson, Fl. 1999

80. Conference on Palliative Care in Pulmonary Disease. Drug Amelioration of Radiation induced fibrosis. Columbia University, NYC, NY 1999

81. American Cancer Society Oncology Update. Aug 2000. Eglin Air Force Base, Ft. Walton Beach, Fl. Melanoma Update.

82. Tumor Board Bayonet point Medical Center, Hyperthermia Nov 2000

83. Columbia University, Center for Life Threatening Illness, Radiation Effects on Pulmonary Function. Nov 2000

84. FDA – Prostate Cancer – Basic Rationale for End Point Analysis. Dec 2000

85. FDA – Exposure Response Relationship in Oncology. Jan 2001

86. USUHS - Chronopharmacology. Feb 2001

87. Bayonet Point Hospital Cancer Conferences – Geriatric Oncology. Sept 2001

88. Columbia University – Pulmonary Effects of Radiation and Quality of Life. Sept 2001

89. Tumor Board Bayonet Point Regional Medical Center. Sarcomas. Nov 2001

90. Tumor Board Bayonet Point Regional Medical Center. Prostate Cancer. Dec 2001.

91. FDA. ASTRO Review-Dec 2001.

92.USUHS-Chronopharmacology. May 2002.

93. Bayonet Point Annual Cancer Conference. Oncologic Emergencies. Sept. 2002.

94. Regulatory Aspects of Chronopharmacology. Bioavailability Conference. San Diego Cal. Jan 2003

95. FDA presentations, CDER, multiple topics on regulatory aspects of drugs, radiation drug interactions and drug study and protocol reviews. 1987-present.

PEER REVIEWED PUBLICATIONS

1. Sokol, G.H., and Maichel, R.P., Studies on rat paw edema induced by S.Aureus, Arch.Int.Pharacodyn.. 1973, 382-385, June 1968.

2. Sokol, G.H. and Maickel, R.P., Toxic interaction of d-amphetamine and tricyclic antidepressants in mice. Res Commun. Chem.Pathol. 3, 513-521, May 1972.

3. Sokol, G.H., Greenblatt, D., et al. Chlordiazepoxide metabolism after hepatic irradiation pharmacology. Pharmacology 3, 248-251, 1975.

4. Sokol, G.H., et al. Complications of lymphangiography in the elderly. Amer.J.Radiol. 43-44, Jan 1977.

5. Sokol, G.H., Greenblatt, D., et al. Effects of abdominal irradiation on drug bioavailability in the human. Journal of Cl.Pharmacology, 388-396, 1978

6. Leuprolide Study Group - Sokol, G.H., Tampa P.I. Leuprolide vs. Diethylstilbestrol for metastatic prostate cancer, N.E.J.M., Vol311, pp 1281-1286, Nov 15 1984.

7. Leuprolide Study Group - Sokol, G.H., Tampa P.I., Clinical effects of Gonadotropin Releasing Hormone Analogue in metastatic carcinoma of the prostate, Urology, Vol.XXV, 2, -106-114, 1985.

8. Cohen, M., Pazdur, R., Sokol, G.H. New Drugs from the FDA. The Oncologist 42-47, Jan 2003

9. Knudsen, J, Sokol, G, and Cantilena, L. Carbonic Anhydrase Activity or Cox-2 inhibitors-A structure activity study. British J. Pharmacology. In press

ABSTRACTS

1. Sokol, G.H., et al. Interaction of adrenergic drugs. Paper presented at American Society of Pharmacology and Experimental Therapeutics, 1968.

2. Sokol, G.H., Greenblatt, D., et al. Effects of abdominal irradiation on drug absorption and bioavailability. Presented 1978 meeting American Society Clinical Pharmacology.

3. Sokol, G.H., Solomon, D., et al. Accuracy of Cytology in Oat Cell Cancer. Accepted for presentation. Published ASCO, Proceedings, May 1980.

4. Paladine, W., Drapkin, R. and Sokol, G.H. - The use of IV Droperidol in Cancer chemotherapy, Published in ASCO, Proc., May 1980.

5. Drapkin, R., McAloon, E., Sokol, G.H., Paladine, W., and Marks, R. The Antiemetic Effects of Dexamethasone in Patients Receiving Cis-Platinum Accepted and Presented, ASCO April 1981.

6. Paladine, W., Ayres, V., Price, L., Drapkin, R., Sokol, G.H., Kritz, E., and Scheinbaum, M. Danazol and Inhibitor of LH and FSH in the Treatment of Recurrent Metastatic Breast Carcinoma. Published ASCO proceedings, 1981.

7. Drapkin, R., Griffith, E., McAloon, E., Palladine, W., Sokol, G.H., Lyman, G., The Tampa Bay Oncology Group. Sequential Methotrexate (MTX) and 5-Flourouracil (5-FU) in Adenocarcinoma of the Colon and Rectum. Published ASCO proceedings, 1981.

8. Sokol, G.H., Drapkin, R., Paladine, W., Price, L., Lyman, G., McCarthy, S., Chadwick, R. The Efficacy of Double Dose Trimethobenzaminde (Tigan) in the Modification of Radiation Induced Nausea—A Double Blind Prospective Randomized Study. Published in ASTR Proceedings, 1981. Presented ASTR Annual Meeting 1981.

9. Sokol, G.H., Saini, D. Scientific Exhibit titled "History of Brachytherapy - Applicators Past and Present," presented at the 1980 ASTR meeting in Dallas. The exhibit was awarded special commendation by the exhibit committee.

10. Huff, W.J., Saini, D.S., Miller, W.M., and Sokol, G.H. Dosimetric Verification of I-125 Dose Calculations in the Prostate Implants. Presented at the twenty-third Annual Meeting of AAPM at Boston, MA

11. LEUPROLIDE THERAPY OF ADVANCED PROSTATE CANCER. L.Michael Globe for the Abbott Prostatic Cancer Study Group. University of Colorado 80262. Published in ASCO Proceeding 1982. Presented ASCO Annual Meeting 1982.

12. Baird, L.C., Greenberg, H., Sokol, G.H. Horseshoe Blocks for isocentric tangential breast Radiotherapy. Accepted for presentation ASTRO 1985 Int.J.Radiation Oncology Aug 1985.

13. Sokol, G.H., Penta, J., McCarthy, S. Phase I Study of Unique C-Parvum Derivative, ASCO Proceedings, C193, p50, 1984.

14. Sokol, G.H., McCarthy, S., and Greenberg, H. Radiation Induced Nausea: The Comparative Efficacy of Oral Metoclopramide versus Prochlorperazine and Placebo. A Double Blind Randomized Study. ASCO Proceedings 1986.

15. Griffith, M.H., and Sokol, G.H. Characteristics of 6MV Photon Beam from a New Linear Accelerator. Presented at International Society of Radiation Oncology.

16. Sokol, G.H., Murgo, A.J., Scully, R., and Justice, R. Analysis of Causes of Clinical "Hold" for Oncology INDs submitted to the FDA. ASCO Proceedings 1992.

17. Sokol, G.H., Murgo, A., Gnecco, C., and Cantilena, L. Does the Cockcroft-Gault

Formula Predict Creatinine in Patients treated with sequential Cisplatin. Abst. and Presentation Proc. Intl. Conf. Clinical Pharmacology 1996

18. Sokol, G.H., Stoeffler, H., Knudsen, J., Cantilena, L. Clinical Pharmacology Outreach
Program: Early Results and Outcomes. Amer.Soc.Clin.Pharm and Therap. Accepted for Presentation March 2000

19. Sokol, G.H., Knudsen, J.F., Murgo, A., Cantilena, L. Utilization of Troponin I as an Index of Chemo/radiotherapy induced cardiac toxicity. Abst. and Presentation American Society of Clin Pharm and Therapeutics, March 2000. To be published in J. Clin. Pharm and Therapeutics Feb 2000.

20. Knudsen, J.F., Sokol, G.H., Cantilena, L. Structure Activity Relationship of the Atypical Antipsychotics with Respect to Thrombotic Activity. Abst. and Presentation American Society of Clin Pharm and Therapeutics, March 2000. To be published in J. Clin. Pharm and Therapeutics Feb 2000.

21. Subramanian, P., Sokol, G.H., Cantilena, L. FDA Pharmacy Quality Assurance Survey – Presented Amer Society Clinical Pharmacology – San Francisco 2002

22. Sokol, G.H., Knudsen, J., Cantilena, L. Appropriateness of Stat and Now Orders. Accepted for presentation, Amer Assoc Clin Pharm. April 2003

23. Knudsen, J., Sokol, G.H. Structure Activity Relationship of Carbonic Anhydrous Inhibitors – Accepted. for presentation, Amer. Soc Clin Pharmacology. April 2003

BOOK CHAPTERS

1. Sokol, G.H., and Maickel, R.P., Editors, Radiation Drug Interactions in Cancer Management, published, Wiley Publisher, Fall 1980.

2. Sokol, G.H., Greenblatt, D., and Kaufman, S., Radiation Effects on the Physiological Dispositions of Drug in Radiation Drug Interactions in Cancer Management. Edited by Sokol, G.H., Maickel, R.P., Wiley Publishers, New York 1980.

3. Sokol, G.H., The Rationale of Combined Modality Treatment of Cancer in Radiation Drug Interactions. Edited by Sokol, G.H., Maickel, R.P., published, Wiley Publisher, Fall 1980.

4. Sokol, G.H., Greenblatt, D., Kaufman, S., Pharmacologic Implications of Radiation Drug Interactions. Textbook Pharmacology, edited by Pradhan, S.N., and Maickel, R.P., Pergamon Press Publisher, to be published 1985.

5. Sokol, G.H., Murgo, A., and Cantilena, L. Geriatric Issues Pertaining to Quality of Life in the Regulatory Evaluation of Drugs - An Oncology Perspective. Accepted for Publication 1997.

OTHER PEER-REVIEWED SCHOLARLY WORKS

1. NDA Review Ifosfamide 1988
2. NDA Review MESNA 1989
3. NDA Supplemental Review MESNA 1999
4. 225 other NDA and IND FDA Reviews, Government Archival Documents Center for Drug Evaluation Research, Rockville, MD 1987- IND Bibliography available on request.
5. NDA Review Mesna tablets 2002 (120 page Government Archival Document)